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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/855,158	05/14/2001	Lars Eyde Theill	A-686A	8931

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EXAMINER

CANELLA, KAREN A

ART UNIT	PAPER NUMBER
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1643

DATE MAILED: 08/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/855,158

Applicant(s)

THEILL ET AL.

Examiner

Karen A. Canella

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 13-17 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☐ Claim(s) 13-17 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|--|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____ | 6) <input type="checkbox"/> Other: ____ |

DETAILED ACTION

1. Claim 13 has been amended. Claims 13-17 are pending and under consideration.
2. Sections of title 35, U.S. Code not found in this action can be found in a prior action.
3. Claims 13-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 recites i. the consensus region of TACI (SEQ ID NO:16); ii. the consensus region of BCMA (SEQ ID NO:7); or iii. the TACI/BCMA extracellular consensus sequence (SEQ ID NO:13) but not the extracellular region of TACI (SEQ ID NO:15) or the extracellular region of BCMA (SEQ ID NO:6). It is unclear if the negative proviso is to be applied to i. and ii. in addition to iii., or if the negative proviso is exclusive to iii. For purpose of examination, the negative proviso will be applied to all of i., ii. and iii.

4. The rejection of claims 13-15 and under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 13 is drawn to a composition of matter, comprising a formula wherein neither X1 nor X2 is naturally occurring and wherein the X groups comprise P1, P2, P3 and P4, wherein each P is independently selected from the consensus region of TACI, the consensus region of BCMA or the extracellular consensus region of TACI/BCMA, wherein P is not the extracellular region of TACI, or the extracellular region of BCMA and wherein each P is linked via an independently selected linker to an Fc domain, a linear polymer, a branched chain polymer, a lipid, a cholesterol group, a carbohydrate, an oligosaccharide, a natural protein, a synthetic protein or a polypeptide which binds to a salvage receptor. The claims encompass a genus of synthetic molecules which minimally comprise the consensus region of TACI, the consensus region of BCMA or the extracellular consensus sequence of TACI/BCMA. Claims 13-15 do not

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limit the functional attributes of the encompassed molecules (it is noted that claim 16 specifies that one of P1 and P2 is a specific binding partner for APRIL and the other is a specific binding partner for AGP-3). One of skill in the art would reasonably conclude that claims 13-15 are not limited to binding to AGP-3 or APRIL. Thus, claims 13-15 encompass a genus of molecules which are highly variant because the genus encompasses molecules which differ substantially in structure from the naturally occurring TACI and BCMA because "P" need only comprise the consensus region of TACI and BCMA. The genus of molecules encompassed by claims 13-15 are also highly variant in terms of function because the claims do not require that the molecules bind to the ligands of AGP-3 and/or APRIL. The disclosure of TACI and BCMA as receptors for AGP-3 and APRIL, and the disclosure that soluble forms of the extracellular portion of the receptor can inhibit binding to the receptor does not adequately describe the claimed genus because the genus encompasses molecules which differ significantly in structure from the extracellular portions of TACI and BCMA as said P groups need only minimally comprise the consensus regions therein thus encompassing other undisclosed proteins which minimally comprise the claimed consensus regions. The disclosure of TACI and BCMA as receptors for AGP-3 and APRIL, and the disclosure that soluble forms of the extracellular portion of the receptor can inhibit binding to the receptor does not adequately describe the claimed genus because the genus encompasses molecules which differ significantly in function from the soluble portion of TACI and/or BCMA because the claims encompass molecules which do not bind to AGP-3 and/or APRIL. One of skill in the art would reasonably conclude that applicant was not in possession of the invention at the time of filing.

5. Applicant argues that the specification describes TACI and BCMA as cell surface receptors of APRIL, and in addition describes molecules which comprise a specific binding partner which binds to a protein of interest such as TACI or BCMA. Applicant argues that the specification describes soluble forms of TACI and BCMA and the TACI-BCMA extracellular consensus sequence as a specific binding partner and the modulation of APRIL and AGP-3 activity by TACI, BCMA APRIL or AGP-3 or portions thereof and therefore adequately describe the genus of claimed products. This has been considered but not found persuasive. It is noted that none of claims 13, 14 or 17 limit the claimed composition in terms of a specific functional

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binding activity; claim 16 mentions that one of P1 and P2 is a specific binding partner for AGP-3 and the other is a specific binding partner for APRIL, but the specific functional activity of the composition of matter as a whole for claim 16 is not a limiting factor in said claim. Further, the disclosure of the extraellular consensus sequence of TACI/BCMA, or consensus regions of TACI and BCMA do not adequately describe the claimed genus, because the claims are drawn to a composition of matter as a whole without limitation of a specific functional activity for the claimed composition which includes a complex combination of structures with variable joining of F1, L1c, L2d, L3e, L1f and P1, P2, P3 and P4. It is further noted that applicant has not disclosed a representative number of species within the claimed genus of the composition.

6. The rejection of claims 13-15 under 35 U.S.C. 103(a) as being unpatentable over Bram et al (WO 98/39361, reference B9 of the IDS filed September 17, 2001) in view of Chaudhary (WO 99/11971, reference B13 of the IDS filed September 17, 2001) is maintained for reasons of record.

Claims 13-15 encompass compositions wherein F1 is a Fc domain, a lipid such as a glycosylphospholipid, or a natural protein such as a transferrin or a hormone or a synthetic protein, and wherein a=1 and b=0 and wherein P is the consensus sequence of TACI with the proviso that X does not comprise a naturally occurring polypeptide.

Bram et al teach chimeric TACI proteins comprising the extracellular domain of a TACI protein linked to the Fc domain of an immunoglobulin a glycosylphospholipid, or a natural protein such as a transferrin, a hormone or a synthetic protein such as the Fv portion of an antibody (page 24, lines 20-34). Bram et al teach synthetic TACI polypeptides comprising a compound of two or more subunit amino acids linked by peptide bonds (page 19, line 33 to page 20, line 1). Bram et al teach that TACI comprises two cysteine rich repeats at residues 33-66 and 70-104 which indicate that TACI is a member of the TNF receptor superfamily (page 4, lines 33-34 and page 19, lines 20-31). Bram et al teach a blocking reagent comprising a recombinant form of the extracellular portion of the TACI receptor which acts to intercept the normal endogenous ligands that crosslink and activate the TACI protein (page 8, lines 1-4). Bram et al do not specifically teach the composition comprising a fragment of the extracellular domain of

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TACI wherein said composition comprises the TACI consensus sequence but does not comprise the entirety of said extracellular domain.

Chaudhary teaches cysteine-rich pseudo repeats in the extracellular domain of the TNF receptor family, wherein said cysteine rich repeats are involved in ligand binding (page 7, lines 24-29).

It would have been prima facie obvious at the time the claimed invention was made to substitute a polypeptide comprising residues 33-104 for the complete extracellular domain in the fusion proteins as taught by Bram et al, and also to make a synthetic polypeptide as taught by Bram et al comprising a cysteine repeat region as a "subunit amino acids" linked by peptide bonds. One of skill in the art would have been motivated to do so by the teachings of Bram et al on the recombinant form of TACI comprising the extracellular portion of TACI which acts to intercept the endogenous ligands of TACI and the teachings of Chaudhary which identify the cysteine repeat regions of members of the TNF-receptor family as important for ligand binding. One of skill in the art would expect that a polypeptide which is shorter than the complete extracellular domain of TACI would be able to intercept exogenous ligands which activate the native TACI receptor as long as said polypeptide comprised the cysteine rich regions identified by Chaudhary as important in ligand binding.

7. The rejection of claims 13-15 under 35 U.S.C. 103(a) as being unpatentable over Shu (U.S. 6,475,987) in view of Chaudhary (WO 99/11971, reference B13 of the IDS filed September 17, 2001) is maintained for reasons of record.

Claims 13-15 encompass compositions wherein F1 is a Fc domain, and wherein a=1 and b=0 and wherein P is the consensus sequence of BCMA, wherein X does not comprise a naturally occurring polypeptide.

Shu teaches that BCMA is a member of the TNF receptor family and that BCMA is the receptor for TALL-1 (column 9, lines 18-43). Shu teaches a method for identifying compounds that regulate the interaction between TALL-1 and its receptor (BCMA) comprising determining whether a putative regulatory compound affects the binding of TALL-1 to the receptor (BCMA) (column 7, lines 3-27). Shu teaches that fusion proteins comprising one or more extracellular domains of BCMA can be used in a non-cell based screening assay to identify compounds for the

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ability to bind to BCMA (column 38, lines 31-35 and 42-46). Shu teaches a composition comprising the extracellular domain of BCMA fused to the Fc domain of an immunoglobulin (column 46, lines 14-18).

Chaudhary teaches cysteine-rich pseudo repeats in the extracellular domain of the TNF receptor family, wherein said cysteine rich repeats are involved in ligand binding (page 7, lines 24-29).

It would have been prima facie obvious at the time the claimed invention was made to substitute a polypeptide comprising the cysteine rich repeats of BCMA for the one or two extracellular domains of BCMA in a fusion protein comprising the immunoglobulin Fc domain as taught by Shu. One of skill in the art would have been motivated to do so by the teachings of Chaudhary which identify the cysteine repeat regions of members of the TNF-receptor family as important for ligand binding. One of skill in the art would expect that a polypeptide which is shorter than the complete extracellular domain of BCMA would function in a assay to identify compounds which bind to the extracellular portion of BCMA

8. Applicant argues that because the '791 publication teaches that the cysteine-rich pseudo repeats in the extracellular domain of TNF receptor superfamily members are involved in ligand binding does not provide motivation for the use of a smaller fragment comprising the cysteine-rich pseudo repeats in lieu of the entire extracellular domain. This has been considered but not found persuasive. It is clear from the teachings of Chaudhary that one of skill in the art would have a reasonable expectation of success in using a smaller fragment than the entire extracellular fragment of TACI because Chaudhary teaches the part of the extracellular portion that is involved in ligand binding. It is noted that only a reasonable expectation of success is required for the rejection under 35 U.S.C. 103(a) Applicant argues that because the '791 publication teaches that the cysteine-rich pseudo repeats in the extracellular domain of TNF receptor superfamily members are involved in ligand binding does not provide motivation for the use of a smaller fragment comprising the cysteine-rich pseudo repeats in lieu of the entire extracellular domain. This has been considered but not found persuasive. It is clear from the teachings of Chaudhary that one of skill in the art would have a reasonable expectation of success in using a smaller fragment than the entire extracellular fragment of TACI because Chaudhary teaches the

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part of the extracellular portion that is involved in ligand binding. It is noted that only a reasonable expectation of success is required for the rejection under 35 U.S.C. 103(a) (M.P.E.P. (2143.02)). Applicant argues that the '791 publication also refers to the entire extracellular domain as the ligand binding domain. This has been considered but not found persuasive. One of skill in the art would know that mention of the entire extracellular domain as the ligand binding domain does not teach against smaller fragments of the extracellular domain for ligand binding because Chaudhary teach the region of the extracellular domain, the cysteine-rich pseudo repeats, which are involved in ligand binding. One of skill in the art upon reading of the Chaudhary publication would readily realize that deletion of some of the amino acid residues from the amino or carboxyl termini of the extracellular domains of either TACI or BCMA, but not deletion of the cysteine-rich pseudo repeats, would result in a ligand that retained the ability to bind to the receptor.

9. All other rejections and objections as set forth in the previous Office action are withdrawn in light of applicants amendments.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 11 am to 10 pm, except Wed, Fri.

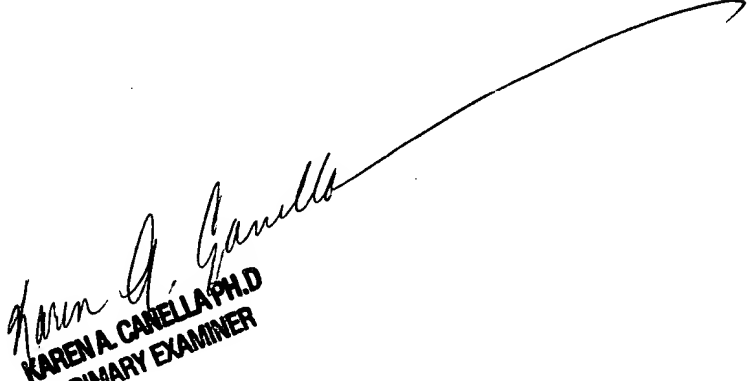
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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.

8/22/2005


KAREN A. CANELLA PH.D.
PRIMARY EXAMINER